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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,959	10/07/2003	Susan Jane Knox	STAN-274	6076

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/680,959	KNOX ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *9-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/17/04 .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election without traverse of Group I, claims 1-8, in the reply filed on June 14, 2004 is acknowledged. The claims of Group II, claims 9-11, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 3 recites a method of protecting normal cells from radiation damage, wherein the cells are contacted with a hyperpolarizing agent immediately after radiation exposure. The specification discloses contacting the cells with a hyperpolarizing agent before exposure to radiation, but not administering the hyperpolarizing agent after exposure to radiation. Thus, the specification does not teach a method of protecting normal cells from radiation in which normal cells are contacted with a hyperpolarizing agent after exposure to radiation. One of ordinary skill in the art would have no

indication that the hyperpolarizing agent could be administered before or after radiation exposure or that administering the hyperpolarizing agent after radiation exposure would be effective in preventing radiation damage. Thus, a holding of non-enablement is required.

Claim 6 recites a method of protecting normal cells from radiation damage in which the radiation is X-rays. There is no disclosure of using X-rays in the specification; only gamma rays (^{137}Cs radiation) are used. X-rays are radiation of a higher energy level that may produce damage to cells that may not necessarily be preventable by treating cells with a hyperpolarizing agent. Thus, the specification does not teach a method of protecting normal cells from radiation in which the radiation is X-rays. One of ordinary skill in the art would have no indication that treating cells with a hyperpolarizing agent would protect the cells from damage caused by exposure to X-rays. Thus, a holding of non-enablement is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites a method of protecting normal cells from radiation damage, but the specification does not define what a normal cell is. The specification discloses practicing the method on three types of stabilized cell lines, rat fibroblasts (Rat-1); SV40-transformed mouse pancreatic endothelial cells (MS1, a cell

line that gives rise to benign hemangiomas- see attached ATCC record for this cell line); and dog kidney epithelial cells (MDCK). Because the term "normal cells" is not defined, the metes and bounds of the claims are unclear, and it cannot be determined what Applicants intend to include in or exclude from the claims. A holding of indefiniteness is therefore required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Fox, Pfluegers Archiv 351(4):303-314, 1974. Fox discloses a method of protecting normal cells (normal neurons) from radiation damage in which the cells are contacted with a hyperpolarizing agent that is effective in hyperpolarizing the cell membrane. The cells are contacted with a phthalic acid buffer at low pH which stops the Na^+ current and blocks the Na^+ channels with protons (H^+). A negative holding membrane potential is created, and the membrane is hyperpolarized. The cells are then irradiated with UV radiation, and decreased sensitivity to radiation is measured in cells with proton-blocked Na^+ channels in the nodal membrane (see p. 304, Methods, and pp. 308-311). Thus, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 5, 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert et al., J Cellular Physiology 168:114-122, 1996. Gilbert discloses a method of protecting cells from radiation damage in which the cells are contacted with a hyperpolarizing agent that is effective in hyperpolarizing the cell membrane. The cells are transfected with an expression vector containing the Bcl-2 gene, effecting expression of the Bcl-2 gene which hyperpolarizes the membrane, or the cells are contacted with valinomycin. Valinomycin opens the K^+/ATP channels, which hyperpolarizes the membrane. The cells are then irradiated, and improved viability is measured in cells treated with either the Bcl-2 expression vector and/or valinomycin

(see p. 115, paragraphs entitled Cell lines and cell culture and Effect of valinomycin on cell viability and membrane potentials, and p. 116, 2d paragraph under Effect of Bcl-2 on radiosensitivity and paragraph entitled Exposure of cells to valinomycin). Gilbert, however, discloses treating the PW and HL60 cell lines, a human B cell lymphoma line and a human leukemia cell line, respectively, and does not disclose treating normal cells. But, Gilbert teaches that hyperpolarizing agents act on the K^+/ATP channels in cell membranes (see p. 118, paragraph entitled Exposure to ouabain) and does not indicate that there are any differences in the K^+/ATP channels between normal cells and PW or HL60 cells. Therefore, one of ordinary skill in the art would have expected, with a reasonable degree of success, that treating normal cells with a hyperpolarizing agent would provide the same protection from radiation as treating PW or HL60 cells. As a result, the skilled artisan would have been motivated to modify the teachings of Gilbert to apply the method to normal cells for the treatment benefits disclosed in the reference (improved radiation resistance). Thus, a holding of obviousness is required.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00 with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner
Art Unit 1651

rk
2004-07-19

FRANCISCO PRATS
PRIMARY EXAMINER